

October 26, 2001

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Sent Via Electronic Mail

Dr. Oscar Hernandez
US EPA Headquarters
401 M Street, SW
East Tower, 104A
Washington, DC 20460

Re: High Production Volume (HPV) Chemical Challenge Program – Test Plan
Submission (CAS # 68608-82-2 and 25340-17-4)

Dear Mr. Hernandez:

The American Chemistry Council Ethylbenzene HPV Task Group¹ submits for review and public comment its test plan, as well as related robust summaries, for the Diethylbenzene-Rich Streams category of chemicals under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program. The Panel understands that there will be a 120-day review period for the test plan and that all comments generated by or provided to EPA will be forwarded to the Panel for consideration.

This test plan for the Diethylbenzene-Rich Streams category addresses two streams that contain a predominance of diethylbenzene isomers (87.6 – 98.8 wt%) and are produced during ethylbenzene manufacture. Samples of the streams will be combined to form a test sample for testing.

Briefly, the test plan for the Diethylbenzene-Rich Streams category includes the following tests:

- o Melting Point
- o Boiling Point
- o Vapor Pressure

¹ The members of the Diethylbenzene-Rich Streams test category are BP Amoco Chemical Company, Chevron Phillips Chemical Company LP, The Dow Chemical Company, Koch Specialty Chemical Company; a Division of Koch Petroleum Group, and Sterling Chemicals, Inc.

- o Partition Coefficient
- o Water Solubility
- o Photodegradation
- o Stability in Water
- o Fugacity Modeling

In the development of this test plan, the Panel considered carefully and tried to limit how many animals might be required for any tests included in the proposed plan and conditions to which the animals might be exposed. As a result, the Panel believes that the concerns of some non-governmental organizations about animal welfare have been fully considered and that use of animals in this proposed test plan has been minimized.

Thank you in advance for your attention to this matter. In contacting this Panel please address Patricia Messenger at (703) 534-3582.

Sincerely yours,

Courtney M. Price,
Vice President, CHEMSTAR

CC: C. Auer, EPA
EB DEB HPV Team

AR201-13 272A

**HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM**

TEST PLAN

For the

Diethylbenzene-Rich Streams Category

Prepared by:

**American Chemistry Council
Ethylbenzene Panel HPV Task Group
Diethylbenzene Subteam**

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October 8, 2001

EXECUTIVE SUMMARY

The Ethylbenzene Panel (Panel) of the American Chemistry Council and the Panel's member companies of the Diethylbenzene-Rich Streams HPV Task Group (Task Group) have committed to develop screening level human health, environmental effects and fate, and physicochemical data for the Diethylbenzene-Rich Streams category under the Environmental Protection Agency's (EPA's) High Production (HPV) Challenge Program (Program).

This test plan for the Diethylbenzene-Rich Streams category addresses two streams that contain a predominance of diethylbenzene isomers (87.4 – 98.8 wt%) and are produced during ethylbenzene manufacture. Samples of the streams will be combined to form a test sample for testing.

Chemical Name	Other Name	CAS No.
Diethylbenzene	Mixed Diethylbenzenes	25340-17-4
Benzene, ethylenated, by-products from	Polyethylbenzenes	68608-82-2

Physical/Chemical Properties

Melting point, boiling point, vapor pressure, partition coefficient, and water solubility of Diethylbenzene-Rich Streams will be evaluated as part of the test plan.

Environmental Fate/Pathways

There is adequate information on the biodegradation of Diethylbenzene-Rich Streams. Since there is inadequate information on photodegradation, stability in water, and transport between compartments (fugacity modeling), these studies will be conducted as part of the test plan.

Ecotoxicity

The existing data on the acute toxicity of Diethylbenzene-Rich Streams to fish, aquatic invertebrates, and aquatic plants are adequate to address the endpoints in the HPV Program. Therefore, no ecotoxicity testing of Diethylbenzene-Rich Streams will be conducted.

Human Health Effects

The existing data on the potential human health hazards of Diethylbenzene-Rich Streams are adequate to address the toxicity endpoints in the HPV Program, including acute oral and dermal toxicity, repeated dose toxicity, *in vitro* and *in vivo* genetic toxicity, and developmental toxicity and reproductive toxicity. Therefore, no toxicity testing of Diethylbenzene-Rich Streams will be conducted.

LIST OF MEMBER COMPANIES
ETHYLBENZENE PANEL
DIETHYLBENZENE HPV TASK GROUP

BP Amoco Chemical Company

Chevron Phillips Chemical Company LP

The Dow Chemical Company

Koch Specialty Chemical Company; a Division of Koch Petroleum Company

Sterling Chemicals Inc.

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TEST PLAN FOR THE DIETHYLBENZENE-RICH STREAMS CATEGORY

1. INTRODUCTION

The Ethylbenzene Panel (Panel) of the American Chemistry Council and the Panel's member companies of the Diethylbenzene-Rich Streams HPV Task Group (Task Group) have committed to develop screening level human health, environmental effects and fate, and physicochemical data for the Diethylbenzene-Rich Streams category under the Environmental Protection Agency's (EPA's) High Production (HPV) Challenge Program (Program).

In preparing this test plan, the Task Group has given careful consideration to the principles contained in the letter EPA sent to all HPV Challenge Program participants on October 14, 1999. As directed by EPA in that letter, the Panel has sought to maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships. Additionally, and also as directed in EPA's letter, the Task Group has conducted a thoughtful, qualitative analysis of the adequacy of existing data. The Task Group has taken the same thoughtful approach when developing its test plan. The Task Group believes its test plan conforms to the principles articulated in EPA's letter.

This plan identifies two CAS numbers used to describe the streams in the category, identifies data of adequate quality for substances included in the category and individual isomers of Diethylbenzene and outlines testing needed to develop screening level data for this category under the Program. This document also provides the testing rationale for the Diethylbenzene-Rich Streams category. The objective of this effort is to identify and develop sufficient test data and/or other information to adequately characterize the human and environmental fate for the category in accordance with the EPA HPV Program.

II. DESCRIPTION OF THE DIETHYLBENZENE-RICH STREAMS CATEGORY

The proposed category is defined as Diethylbenzene-Rich Streams. This category consists of streams that contain a predominance of diethylbenzene isomers and are produced during ethylbenzene manufacture.

Ethylbenzene is produced through alkylation of benzene with ethylene. In addition to the production of ethylbenzene, there are side reactions that involve the reaction of ethylene with ethylbenzene to produce diethylbenzene, and, to a much lesser extent, further

alkylations to produce triethylbenzene and polyethylbenzene. In addition, butylbenzene and other alkylaromatics may be formed in varying limited amounts. After the ethylbenzene is removed, the remaining stream is separated into a diethylbenzene-rich stream and a bottoms stream. Some manufacturers may further process the diethylbenzene-rich streams to increase the diethylbenzene content. The diethylbenzene-rich streams are identified by two CAS Registry Numbers:

Chemical Name	Other Name	CAS No.
Diethylbenzene	Mixed Diethylbenzenes	25340-17-4
Benzene, ethylenated, by-products from	Polyethylbenzenes	68608-82-2

The composition of both diethylbenzene-rich streams is listed below based on capillary GC analysis of samples submitted by the four participating companies to BP Amoco Analytical Technology (BP Amoco, 2000).

Component	Wt %
Diethylbenzenes ^a	87.6 – 98.8
Triethylbenzenes	<5.1
Polyethylbenzenes	<0.1
Iso-/sec-butylbenzenes	0.6 – 1.1
Other alkylbenzenes	0.7 – 4.5
Ethylbenzene	<1.9
Benzene	<0.1
Diphenylalkanes	<0.1
Ethyl diphenylethanes and Diethyl biphenyls	<0.1
PNAs (3-rings)	<0.1
Paraffins/Naphthenes	<1.6
Total of unidentified components, each present at <0.1%	<1.4

^an-butylbenzene coeluted with 1,4-diethylbenzene

As shown in the table above, the range of composition for both Diethylbenzene-Rich Streams (CAS No. 25340-17-4 and CAS No. 68608-82-2) are very similar. For purposes of the proposed testing, equal quantities of the streams from each of the four sponsoring companies will be combined to form a representative test sample of Diethylbenzene-Rich Streams.

III. SUMMARY OF EXISTING INFORMATION AND TEST PLAN RATIONALE

Existing information on Diethylbenzene-Rich Streams and diethylbenzene isomers is summarized below. The SIDS endpoints with sufficient data for the HPV program are summarized in Appendix 1.

A. Physical/Chemical Properties

Melting point, boiling point, vapor pressure, partition coefficient, and water solubility of Diethylbenzene-Rich Streams will be evaluated as part of the test plan.

There are reported data for these endpoints for diethylbenzene isomers but not for Diethylbenzene-Rich Streams (HSDB, 2001).

	1,2-Diethylbenzene	1,3-Diethylbenzene	1,4-Diethylbenzene
Boiling Point (°C)	184	181.1	183.7
Melting Point (°C)	-31.2	-83.9	-42.83
Vapor Pressure (mm Hg at 25 °C)	1.05	1.20	1.03
Water Solubility (mg/l at 25 °C)	71.1	24.0	24.8
Octanol/Water Partition Coeff. (log K _{ow})	3.72	4.44	4.45

B. Environmental Fate/Pathways

There is adequate information on the biodegradation of Diethylbenzene-Rich Streams. Since there is inadequate information on photodegradation, stability in water, and transport between compartments (fugacity modeling), these studies will be conducted as part of the test plan.

1. Biodegradation

In a CO₂ evolution test using unacclimated microbial cultures, Mixed Diethylbenzenes degraded 4.7% after 28 days and 5.5% after 35 days, indicating that it is not readily biodegradable (Marks et al., 1995). Similar results were obtained for 1,4-diethylbenzene (MITI, 1993; SIDS Dossier, 1994; SIDS SIAR, 1994). However, acclimated microorganisms completely degraded all three isomers of diethylbenzene at low concentrations (≤ 0.5 mg/l in about 5 days (MHW, 1993c; SIDS Dossier, 1994; SIDS SIAR, 1994; HSDB, 2001).

2. Photodegradation

All three isomers have been reported to photodegrade (HSDB, 2001).

3. Bioaccumulation

A bioaccumulation study in carp demonstrated a moderate potential of 1,4-diethylbenzene to bioconcentrate based on bioconcentration factors (BCF) of 320-629 (MITI, 1992; SIDS Dossier, 1994; SIDS SIAR, 1994).

C. Ecotoxicity

The existing data on the ecotoxicity of Diethylbenzene-Rich Streams are adequate to address the endpoints in the HPV Program. Therefore, no ecotoxicity testing of Diethylbenzene-Rich Streams will be conducted.

Mixed Diethylbenzenes was slightly toxic to fish, daphnids, and algae. The LC50 value was 23 mg/l for rainbow trout (Ward et al, 1996a). EC50 values of 39 mg/l (Ward et al., 1996b) and 9.42 mg/l (Tucker et al., 1987a) were reported for *Daphnia magna*. The 96 hour EC50 for the algae *Selenastrum capricornutum* was reported as 47 mg/l (Ward et al, 1996c) and greater than 20.06 mg/l (Tucker et al., 1987b).

1,4-Diethylbenzene was moderately toxic to fish and daphnids, and slightly toxic to algae (EA, 1992; SIDS Dossier, 1994; SIDS SIAR, 1994). The 96-hour LC50 for red killitish was 1.8 mg/l, the 24 hour EC50 for *Daphnia magna* was 32.0 mg/l, and the 72 hour EC50 in the algae *Selenastrum capricornutum* was 29 mg/l. In a daphnid 21-day reproduction study, 1,4-diethylbenzene did not show a tendency for cumulative chronic toxicity: the 48-hour LC50 was 6.0 mg/l; at 21 days, the LC50 was 2.4 mg/l, the reproduction EC50 was 1.3 mg/l, the reproduction LOEC was 3.0 mg/l and the reproduction NOEC was 0.93 mg/l.

D. Human Health Effects

The existing data on the potential human health hazards of Diethylbenzene-Rich Streams are adequate to address the toxicity endpoints in the HPV Program. Therefore, no toxicity testing of Diethylbenzene-Rich Streams will be conducted.

1. Acute Toxicity

Diethylbenzene-Rich Streams are characterized by low acute oral and dermal toxicity. Oral LD₅₀ of 2050 to 6900 mg/kg have been reported for Mixed Diethylbenzenes (Chevron, 1991a; Biodynamics, 1987a). In two studies with Mixed Diethylbenzenes, the dermal LD₅₀ was reported to be greater than 2000 mg/kg in rats (Chevron, 1991 b) and greater than 5000 mg/kg in rabbits (Biodynamics, 1987b).

The oral LD50 for 1,4-diethylbenzene was greater than 2000 mg/kg in Sprague-Dawley rats (MHW, 1993a; SIDS Dossier, 1994; SIDS SIAR, 1994).

Mixed Diethylbenzenes caused reversible moderate skin irritation (average scores at 24, 48, and 72 hours were 3.1 for erythema and 0.4 for edema; Draize score of 3.4 of a possible 8.0 after a 4-hour exposure) (Chevron, 1990a) and slight to moderate conjunctival irritation (Draize score of 2.7 of a possible 110) (Chevron, 1990b). Mixed Diethylbenzenes tested by Monsanto (1992) caused similar eye and skin irritation. Mixed Diethylbenzenes were negative for skin sensitization potential (Chevron, 1991c).

2. Subchronic Toxicity

Rats were exposed by inhalation to Mixed Diethylbenzenes at 0, 190, 610 and **1400** mg/m³ for 10 weeks, six hr/day, five days per week (Kaempfe and Thake, 1993). The NOAEL was 190 mg/m³. Mean body weights were observed in the high-dose group throughout the study. There were no treatment-related abnormal clinical observations or ocular abnormalities. Treatment-related changes in hematologic parameters included moderate decreases in total white cell and lymphocyte counts in the mid- and high-exposure level males. Abnormal sera color (blue or blue-gray) was observed in high-exposure level males and females. Treatment-related changes in serum chemistry parameters included decreases in alanine aminotransferase, aspartate aminotransferase and creatinine phosphokinase in high-exposure level females and increases in potassium in high-level males and phosphorus in males from the high-exposure group and females from the mid- and high-exposure groups. An abnormal blue-gray color was observed in most tissues from all but one high-exposure animal. At the mid-exposure level, the same color was observed in brains and in the urinary bladders of some animals. This abnormal color probably resulted from the presence of the parent chemical or a metabolite in these tissues. There were no other gross or macroscopic changes attributed to the test material, including no effects on reproductive organs of either sex.

Rats were exposed orally to 1,4-diethylbenzene at 0, 30, 150 or 750 mg/kg/day for 28 days in the combined repeat dose and reproductive/developmental toxicity screening test (MHW, 1993a; SIDS Dossier, 1994; SIDS SIAR, 1994). Effects were noted in the livers (increased weights, brown color, and swollen cells) and kidneys (increased weights), with corresponding effects noted in the blood chemistries; however, there were no corresponding histopathologic findings. The no effect level (NOEL) was determined to be 30 mg/kg/day.

3. Neurotoxicity

Subchronic oral studies of Mixed Diethylbenzenes and diethylbenzene isomers which focused on neurotoxicity have been conducted (Gagnaire et al., 1990). Mixed Diethylbenzenes were administered at 0, 500 or 7.50 mg/kg/day for 10 weeks, 5 days/week. In both treated groups, rats exhibited a blue discoloration of the skin and urine and two animals in each group died during the study. A significant reduction in body weight gain was observed from the first week in the high-dose group. Rats in the treated groups developed severe weakness in hind limbs and disturbances in gait that resulted in a complete paralysis of the hind limbs for some rats. There was a time-dependent decrease in motor conduction velocity, sensory conduction velocity and amplitude of the sensory action potential. The LOAEL was 500 mg/kg.

In the studies of the isomers, 1,2-diethylbenzene was administered at 100 mg/kg/day, 4 days/week for 8 weeks, whereas 1,3-diethylbenzene and 1,4-diethylbenzene were each administered at 500 mg/kg/day to rats for five days/week for 8 weeks (Gagnaire et al., 1990). There was an eight-week post-exposure observation period for the isomer studies. Rats given 1,2-diethylbenzene developed the same symptoms (decreased body weight,

blue discoloration of the skin and urine, weakness of hind limbs, paralysis) as those described for the diethylbenzene mixture. Two rats died during the study. 1,3-Diethylbenzene and 1,4-diethylbenzene-treated rats did not display any signs of neurotoxicity or any other signs of systemic toxicity. During the recovery period, the 1,2-diethylbenzene treated rats regained weight and became more mobile, but presented trailing hind limbs when attempting to walk. On the 4th week of recovery, all animals treated with 1,2-diethylbenzene succeeded in standing up. A time-dependent decrease in motor conduction velocity, sensory conduction velocity and amplitude of the sensory action potential was observed in animals dosed with 1,2-diethylbenzene but not with 1,3- or 1,4-diethylbenzene. The LOAEL for 1,2-diethylbenzene was 100 mg/kg whereas the NOAEL was 500 mg/kg for 1,3- and 1,4-diethylbenzene.

In additional neurotoxicity evaluations, rats were exposed to a commercial mixture of diethylbenzene isomers by inhalation at approximately 500, 600, 700, 800 or 900 ppm for 6 hrs/day, 5 days/week, for 18 weeks (Gagnaire et al., 1992a). There were treatment-related weakness or paralysis of the hindlimbs and disturbance of gait (not observed at 500 ppm), changes in motor and sensory nerve conduction velocities, changes in amplitude of the sensory action potential, and/or changes in parameters of the brainstem auditory evoked potential. Thus, in these studies, diethylbenzene was neurotoxic following repeated exposure to high levels. Rats exhibited a blue discoloration of tissues and urine. A NOEL was not determined, but the lack of clinical signs at 500 ppm indicates a decreased response at that exposure level.

When administered by ip injection 4 days/week at 10 mg/kg for 11 weeks or at 2 mg/kg for 6 weeks, the metabolite 1,2-diacetylbenzene caused hindlimb weakness at 10 mg/kg, hindlimb weakness and disturbance in gait at 20 mg/kg, and a decrease in mean sensory and motor conduction velocities at both dose levels (Gagnaire et al., 1991).

In another study, 1,2-diethylbenzene administered orally at 75 and 100 mg/kg/day, 4 days/week for 8 weeks, and intraperitoneal injection of 1,2-diacetylbenzene at 10 or 15 mg/kg/day, 4 days/week for 8 weeks, produced time- and dose-dependent alteration in brainstem auditory evoked potentials which did not completely recover during an 8 or 10 week recovery period (Gagnaire et al., 1992b).

4. Genetic Toxicity

Mixed Diethylbenzenes was negative for the reverse mutation assay with *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA 1537 with and without S-9 activation (Chevron, 1991d; Stankowski, 1988), and with *E. coli* WP2 uvrA with and without S-9 activation (Chevron, 1991d). Mixed Diethylbenzenes was also negative in an *in vivo* micronucleus study in which mice were dosed intraperitoneally with 1000, 2000, or 4000 mg/kg (Chevron, 1991 e). In a chromosomal aberration study using Chinese hamster ovary cells, Mixed Diethylbenzenes was negative with and without S-9 activation (Myers and Fahey, 1989).

1,4-Diethylbenzene was also negative in a bacterial reverse mutation assay (*Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TAI 538, and *E. coli* uvrA with and without metabolic activation) (MHW, 1993b; SIDS Dossier, 1994; SIDS SIAR, 1994). It was also negative in a Chinese hamster CHL cytogenetics assay with and without metabolic activation (MHW, 1993b; SIDS Dossier, 1994; SIDS SIAR, 1994).

5. Developmental Toxicity

Mixed Diethylbenzenes administered orally to pregnant rats on gestation days 6-16 at 20, 100 and 200 mg/kg did not cause birth defects or developmental variations (Mercieca, 1992). The NOEL for maternal toxicity (reduced body weights and food consumption) was 20 mg/kg, whereas the NOEL for fetal body weight effects was 100 mg/kg. Mixed Diethylbenzenes streams was not teratogenic in this study.

1,2-Diethylbenzene was administered orally to pregnant Sprague-Dawley rats at 0 (corn oil vehicle), 5, 15, 25 and 35 mg/kg on gestation days 5-20 (Saillenfait et al., 1999). Maternal weight gain and food consumption were decreased in the rats that received 15, 25 and 35 mg/kg. There was no effect on number of live fetuses, implantations, non-surviving implantations per litter, or fetal sex ratios. Fetal body weights were reduced in a dose-related fashion in the groups receiving 15, 25 and 35 mg/kg. The NOEL for both maternal and fetal toxicity was 5 mg/kg. There was no treatment-related effect on external visceral and skeletal malformations. 1,2-Diethylbenzene was not teratogenic in this study.

6. Reproductive Toxicity

In the subchronic inhalation study reported by Kaempfe and Thake, 1993 (see above), rats exposed by inhalation to Diethylbenzene-Rich Streams at 0, 190, 610 and 1400 mg/m³ for 10 weeks, six hr/day, five days per week had no effects on reproductive organs of either sex.

Sprague-Dawley rats were dosed orally with 1,4-diethylbenzene at 0, 30, 150 or 750 mg/kg/day in the combined repeat dose and reproductive/developmental toxicity screen level (MHW, 1993a; SIDS Dossier, 1994; SIDS SIAR, 1994). Males were dosed for 44 days, including 14 days before mating and females from 14 days before mating until Day 3 of lactation. There were no effects on mating, fertility, estrus cycle, pup body weight, or gross abnormalities at any dose. A slight increase in duration of gestation and a slight decrease in viability index at Day 4 in male pups in the 750 mg/kg/day group were not considered treatment-related by the investigators.

Based on the lack of effects on reproductive organs in the subchronic inhalation study (Kaempfe and Thake, 1993) and the availability of the developmental study (Mercieca, 1992) as well as the reproduction screen with 1,4-diethylbenzene, there is sufficient information on reproduction endpoints for the HPV program.

7. Toxicokinetics

In pregnant Sprague-Dawley rats given a single oral dose of 25 mg/kg, [¹⁴C] 1,2-diethylbenzene concentrations in the fetus measured at 28-60% of the levels in maternal plasma within the first 48 hours after dosing and were consistently lower than levels in the placenta (Saillenfait et al., 1999). Placental and fetal tissues accounted for < 0.35% of the administered dose. Thus, there was limited placental transfer to the developing rat Fetus.

Gagnaire et al. (1991) reported 1,2-diacetylbenzene in urine from rats given 165 mg/kg 1,2-diethylbenzene orally on four consecutive days. In male Sprague-Dawley rats administered [¹⁴C] 1,2-diethylbenzene intravenously (1 mg/kg) or oral (1 or 100 mg/kg), radioactivity was rapidly absorbed and mainly excreted in the urine (6576% of the dose), and to a lower extent in the feces (15-23% of the dose) or via exhaled air (3-5% of the dose) (Payan et al., 1999). Biliary metabolites were extensively reabsorbed from the gut and ultimately excreted in urine. The two main metabolites were two glucuronide conjugates, probably of the two enantiomers of 1-(2'-ethylphenyl) ethanol, suggesting that the main initial conversion step of the primary metabolic pathway appears to be the hydroxylation of the α -carbon of the side chain. In this study, insignificant amounts of the neurotoxic metabolite 1,2-diacetylbenzene were detected in urine, bile and feces. Payan et al. (2001) reported that the two main metabolites of 1,2-diethylbenzenes in urine of treated rats are the glucuronide conjugates of two enantiomers of 1-(2'-ethylphenyl)ethanol. The metabolic steps which lead to the conjugates are under stereoselective control.

8. Carcinogenicity

A study of the dermal carcinogenesis potential of diethylbenzene (composition not given) (10% in acetone) applied to the backs of C3H/HEJ mice found one squamous cell carcinoma whereas none were reported in control mice (BRRC, 1983). Historical control data were not presented.

IV. TEST PLAN SUMMARY

HPV Category: Diethylbenzene Streams
(CAS No. 25340-17-4 and CAS No. 68608-82-2)

Adequate information is available to address the following HPV endpoints:

	Adequate Data Available
3.5	Biodegradation
4.1	Acute Toxicity to Fish
4.2	Acute Toxicity to Aquatic Invertebrates
4.3	Toxicity to Aquatic Plants (e.g. Algae)
5.1.1	Acute Oral Toxicity
5.1.3	Acute Dermal Toxicity
5.4	Repeated Dose Toxicity
5.5	Genetic Toxicity <i>In Vitro</i>
5.6	Genetic Toxicity <i>In Vivo</i>
5.9	Developmental Toxicity/Teratogenicity
5.8	Reproductive Toxicity

The study plan for Diethylbenzene-Rich Streams will address the following HPV endpoints:

	Inadequate Data and/or Datagaps
2.1	Melting Point
2.2	Boiling Point
2.4	Vapor Pressure
2.5	Partition Coefficient
2.6	Water Solubility
3.1.1	Photodegradation
3.1.2	Stability in Water
3.3.1	Fugacity Model I or III

V. REFERENCES

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Ward, T. J., Magazu, J. P., and Boeri, R. L., 1996b. Acute toxicity of polyethylbenzene polyethylbenzene [Mixed Diethylbenzenes] to the daphnid, Daphnia. magna. Wilbury Laboratories, Inc. Study Number 774-CH. Conducted for Chevron Research and Technology Co., Richmond, California.

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Appendix 1: Summary of HPV Endpoints with Existing Sufficient Information for Diethylbenzene-Rich Streams

HPV SIDS Endpoints	Test Material*	Data Summary	Reference
3.5 Biodegradation	1	Not readily biodegradable. 4.7% after 28 days; 5.5% after 35 days	Marks et al., 1995
4.1 Acute Toxicity to Fish	1	96-hour LC ₅₀ = 23 mg/liter NOEC (96 hour) = 13 mg/liter	Ward et al., 1996a
4.2 Acute Toxicity to Aquatic Invertebrates	1	(A) EC ₅₀ = 39 mg/liter NOEC (48 hour) < 13 mg/liter (B) EC ₅₀ = 9.42 mg/liter	(A) Ward et al., 1996b (B) Tucker et al., 1997
4.3 Toxicity to Aquatic Plants (e.g., Algae)	1	(A) Growth rate (72 and 96 hr): EC ₅₀ = 63 and 66 mg/l; NOEC = 25 mg/l Cell density (72 and 96 hr): EC ₅₀ = 41 and 47 mg/l; NOEC = 13 and 25 mg/l (C) Biomass effects (96 hr): EC ₅₀ = >20.06 mg/l	(A) Ward et al., 1996c (B) Tucker et al., 1997
5.1.1 Acute Oral Toxicity	1	(A) Rat LD ₅₀ = 2050 mg/kg (both sexes) (B) Rat LD ₅₀ = 6900 mg/kg (males) and 4700 mg/kg (females)	(A) Biodynamics, 1987 (B) Chevron, 1991a
5.1.3 Acute Dermal Toxicity	1	(A) Rabbit LD ₅₀ = >5000 mg/kg (B) Rat LD ₅₀ = >2000 mg/kg	(A) Biodynamics, 1987 (B) Chevron, 1991b
5.4 Repeated Dose Toxicity	1,2,3	(A) NOAEL = 190 mg/m ³ (B,C) Specialized neurotoxicity studies: Oral: LOAEL = 500 mg/kg/day Inhalation: LOAEL = 500 ppm	(A) Kaempfe and Thake, 1993 (B) Gagnaire et al., 1990 (C) Gagnaire et al., 1992a
5.5 Genetic Toxicity <i>In Vitro</i>	1	(A, B) Negative for bacterial mutations (C) Negative for chromosomal aberration in Chinese hamster ovary cells	(A) Chevron et al., 1991a (B) Stankowski, 1988 (C) Myers and Fahey, 1989
5.6 Genetic Toxicity <i>In Vivo</i>	1	Negative for micronuclei in bone marrow erythrocytes	Chevron, 1991e

Appendix 1 (continued): Summary of HPV Endpoints with Existing Sufficient Information for Diethylbenzene-Rich Streams

HPV SIDS Endpoints	Test Material*	Data Summary	Reference
5.8 Reproductive Toxicity	1,3	(A) No effect on reproductive organs in subchronic study (B) Reproduction screen with 1,4-diethylbenzene. NOAEL = 750 mg/kg/day	(A) Kaempfe and Thake, 1993 (B) MHW, 1993a; SIDS Dossier, 1994; SIDS SIAR, 1994
5.9 Developmental Toxicity	1,3	(A) Rat oral gavage with Mixed Diethylbenzenes Maternal NOAEL = 20 mg/kg/day Developmental NOAEL = 100 mg/kg/day (B) Rat oral gavage with 1,2-DEB Maternal NOAEL = 5 mg/kg/day Developmental NOAEL = 5 mg/kg/day	(A) Mercieca, 1992 (B) Saillenfait et al., 1999

*Test Material code:

1 = Mixed Diethylbenzene Stream (CAS No. 25340-17-4)

2 = Diethylbenzene isomers (mixed)

3 = 1,2- or 1,3- or 1,4-diethylbenzene

A 2201-13272 B

**HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM**

ROBUST SUMMARIES

**For the
Diethylbenzene-Rich Streams Category**

Prepared by:

**American Chemistry Council
Ethylbenzene Panel HPV Task Group
Diethylbenzene Subteam**

September 18, 2001

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BIODEGRADATION

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No.25340- 17-4)
Purity: Not specified
Remarks:

Method

Method/guideline followed: EC Method C. 4-C, 1992
Type: CO₂ evolution test (aerobic)
GLP: Yes
Year: 1995
Contact time: 35 days
Innoculum: Activated sludge

Remarks: The test apparatus consisted of six glass 4-liter Erlenmeyer flasks containing two liters of modified biochemical oxygen demand (BOD) water. The test system was activated sludge collected from the Downingtown Regional Water Pollution Control Center (Pennsylvania) and screened through a 2 mm sieve and adjusted to a target solids level of 2500 mg/liter by diluting with settled sludge effluent. The adjusted sludge was aerated in semi-continuous activated sludge (SCAS) units until used in the preparation of the inoculum added to all flasks (up to 24 hours prior to study initiation). The sludge was not exposed to the test substance in the laboratory prior to addition to the test flasks. Test substance was added directly to the flasks to a final concentration of 10 mg/liter. The flasks were placed on a rotary platform shaker and mixed at 110 ± 10 rpm for the duration of the study. Incubation temperature was 22.2 to 23.2 °C.

Results

Degradation % after time: 4.7 after 28 days; 5.5 after 35 days
Results: Mixed diethylbenzene stream is not readily biodegradable.
Kinetics: Not determined
Breakdown products: Not determined

Remarks:

Conclusions

The biodegradation of mixed diethylbenzene under aerobic conditions has been adequately characterized.

Data Quality

Reliability (Klimisch):

1B

Remarks:

Reliable without restriction; comparable to guideline study.

References

Marks, K. H., Crapo, K. C. and Doi, J. (1995). EC: CO₂ Evolution Test on Polyethylbenzene [Mixed Diethylbenzenes]. Unpublished Report by Roy F. Weston, Inc, Study No. 95-056. Conducted for Chevron Research and Technology Company.

Other Available Reports

MITI, Japan. 1993. Unpublished Report [1,4-Diethylbenzene]. Test was performed in Chemicals Inspection and Testing Institute.

4B: Not assignable; only secondary literature.

Other

Last changed:

September 4, 2001

Remarks:

ACUTE/PROLONGED TOXICITY TO FISH

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No.25340-17-4)
Purity: Not specified
Remarks:

Method

Method/guideline followed: OECD Method No. 203
Type: Static
GLP: Yes
Year: 1995
Species/Strain/Supplier: *Oncorhynchus mykiss* (rainbow trout)/Mount Lassen Trout Farm, Red Bluff, California
Analytical monitoring: No
Exposure period: 96 hours
Statistical methods: Computerized program developed by Stephen et al. that uses the probit method to calculate the LC₅₀ and 95% confidence limits.

Remarks: All fish were held in culture tanks on a 16-hour daylight photoperiod and observed for at least 14 days prior to testing. Ten fish per concentration were exposed to nominal test concentrations of 0 (dilution water control), 13, 22, 36, 60, and 100 mg/l mixed diethylbenzene stream, in two replicates. Fish were fed standard commercial fish food (Tetra Min[®] Staple Food) daily until 48 hours prior to testing, at which time feeding was discontinued. Observations were made at 24, 48 and 96 hours. The bioassay was conducted in 20-liter glass vessels containing 15 liters of test solution. Appropriate amounts of the test substance were added directly to dilution water in test vessels. Water had a hardness of 44 mg/liter and an alkalinity of 35 mg/liter as CaCO₃. The mean dissolved oxygen concentration during the study was 9.1 mg/liter (range = 7.3 to 10.4 mg/liter), the mean conductivity was 170 µmhos/cm (range = 160 to 180 µmhos/cm), the mean temperature was 12.0°C (range = 11.1 to 12.8°C), and the pH ranged from 6.6 to 7.4. At the conclusion of the test, the control fish had an average total length of 50.7 mm (range = 46.1 to 56.4 mm) and an average wet weight of 1.19 g (loading rate was approximately 0.79 g/liter).

Results

Nominal concentrations (mg/l): 0, 13, 22, 36, 60, and 100
Measured concentrations (mg/l): not measured
Unit: mg/l
Element value: 96-hour LC₅₀

Statistical results:	= 23 mg/l
Remarks:	NOEC (96 h) was 13 mg/l. In soluble material was noted on the surface of the \geq 22 mg/liter media throughout the exposure period, and in the 13 mg/liter media at the start of the test (0 to 4 hours). No fish died in the 0 and 13 mg/l dose groups at 24, 48 and 96 hours. The 100 mg/l dose group had 100% mortality by 24 hours. The NOEC (96 h) was 13 mg/l. The 96-hour LC ₅₀ was 23 mg/l and the 95% confidence interval = 20 to 26 mg/l.
Conclusions	The acute toxicity to fish has been adequately characterized by this study.
Data Quality	
Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; OECD guideline study.
References	Ward, T. J. , Magazu, J. P., and Boeri, R. L. 1996. Acute Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] to the Rainbow Trout, <i>Oncorhynchus mykiss</i> . Unpublished Report by T. R. Wilbury Laboratories, Inc. Study No. 773-CH. Conducted for Chevron Research and Technology Company.
Other Available Reports	Japanese Environmental Agency. 1992. Investigation of the Ecotoxicological Effects of OECD High Production Volume Chemicals [Acute Toxic Test by Fish (<i>Oryzias latipes</i>) on 1,4-diethylbenzene]. 4B: Not assignable; on secondary literature.
Other	
Last changed:	September 4, 2001
Remarks:	

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (A)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-1 7-4)
Purity:
Remarks:

Method

Method/guideline followed: OECD Method No. 202
Test type: Static
GLP: Yes
Year: 1995
Analytical procedures: None
Species/Strain: *Daphnia magna* (Daphnid)
Test details: Nominal concentrations were 0, 13, 22, 36, 60, and 100 mg/l.

Statistical methods: Computerized program developed by Stephen et al., which calculated the EC₅₀ and 95% confidence by the binomial/nonlinear interpolation method.

Remarks: The *Daphnia magna* used in the test were cultured at the T. R. Wilbury Laboratories, Inc. facilities. Daphnids (less than 24 hours old) were exposed to nominal concentrations of 0, 13, 22, 36, 60, or 100 mg/liter mixed diethylbenzene mixture in a 48-hour static acute toxicity test. Prior to the test, adult daphnids were supplied with the freshwater alga, *Selenastrum capricornutum*, and a yeast/trout chow mixture daily. Ten daphnids were used at each concentration in two replicates. Testing was carried out in 300 ml glass beakers containing 250 ml of test solution or dilution water. These vessels were kept at 20 (±2.0)°C. The lighting was maintained by cool-white fluorescent light on a 16-hour daylight photoperiod, providing a light intensity of 1-4 µEin/m²sec. Water had a hardness of 164 mg/liter and an alkalinity of 108 mg/liter as CaCO₃. The mean dissolved oxygen concentration during the study was 8.6 mg/liter (range = 8.2 to 8.9 mg/liter), the mean conductivity was 590 µmhos/cm (range = 580 to 620 µmhos/cm), the mean temperature was 20.2°C (range = 19.8 to 20.9°C), and the pH ranged from 8.0 to 8.3.

Results

Nominal concentrations (mg/l): 0, 13, 22, 36, 60, and 100
Measured concentrations (mg/l): not determined
Unit: mg/l
EC₅₀ (48 hour): = **39** mg/l
NOEC (48 hour): <**13** mg/l
Statistical results:

Remarks:	Insoluble material was noted on the surface of the 60 and 100 mg/liter media at 24 hours. The 100 mg/l dose group had 100% mortality during the 2-4 hour time period, with the replicate study having 20% survival rate. The 48-hour LC ₅₀ was 39 mg/l with a 95% confidence interval of 22 to 60 mg/l. The NOEC was less than 13 mg/l. The control response was satisfactory.
Conclusions	The acute toxicity to aquatic invertebrates has been adequately characterized by this study.
Data Quality	
Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; OECD guideline study.
References	Ward, T. J. , Magazu, J. P., and Boeri, R. L. 1996. Acute Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] to the Daphnid, <i>Daphnia magna</i> . Unpublished Report by T. R. Wilbury Laboratories, Inc. Conducted for Chevron Research and Technology Company.
Other Available Reports	Tucker, M. W., Adams, W. J., and Kimerle, R. A. 1987. A Measure of the Acute Toxicity of MCS 23 13 (Therminol LT) to <i>Daphnia magna</i> . Monsanto Environmental Sciences Center Report No. ESC-EAG-87-97. 2C: Reliable with restrictions; comparable to guideline study with acceptable restrictions. Japanese Environmental Agency. 1992. Investigation of the Ecotoxicological Effects of OECD High Production Volume Chemicals [Daphnia sp., Acute Immobilisation Test and Reproduction Test on 1,4-diethylbenzene]. 4B: Not assignable; only secondary literature.
Other	
Last changed:	September 4, 2001
Remarks:	

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (B)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340- 17-4)
Purity:
Remarks:

Method

Method/guideline followed: Not stated
Test type: Static
GLP: No
Year: 1987
Analytical procedures: None
Species/Strain: *Daphnia magna* (Daphnid)
Test details:
Statistical methods: Computerized program developed by Stephen *et al.*, which calculated the EC₅₀ and 95% confidence levels. The *Daphnia magna* used in the test were cultured at the Monsanto Environmental Sciences Center facilities. Daphnids (less than 24 hours old) were exposed to test material in a 48-hour static acute toxicity test. Stock solution of the test material was prepared by adding 203.1 mg test material into a volumetric flask and adding dimethylformamide to a final volume of 10 ml. For each test concentration, the appropriate amount of stock solution was added into 1000 ml of dilution water. The maximum amount of solvent used in this test was 0.5 ml/liter of dimethylformamide. Prior to the test, adult daphnids were fed a trout chow solution and algae three times per week. Ten daphnids were used at each concentration. Testing was carried out in 250 ml glass beakers containing 200 ml of test solution or dilution water. These vessels ranged from 2.14 to 22.7°C. The lighting was maintained by cool-white fluorescent light on a 16-hour daylight photoperiod. Alkalinity ranged from 222 to 240 mg/liter; the hardness ranged from 154 to 166 mg/liter; the pH ranged from 8.5 to 8.7; and the dissolved oxygen ranged from 8.8 to 9.2 mg/liter.
Remarks:

Results

Nominal concentrations (mg/l):
Measured concentrations (mg/l): not determined
Unit: mg/l
EC₅₀ (48 hour): = 9.42 mg/l (95% confidence range: 5.00 to 9.99 mg/l)
NOEC (48 hour):
Statistical results:
Remarks:

Conclusions

Data Quality

Reliability (Klimisch):
Remarks:

2 c
Reliable with restrictions; comparable to guideline study with acceptable restrictions.

References

Tucker. M. W., Adams, W. J., and Kimerle, R. A.
1987. A Measure of the Acute Toxicity of MCS 23 13 (Therminol LT) to *Daphnia magna*. Monsanto Environmental Sciences Center Report No. ESC-EAG-87-97.

Other Available Reports

Ward, T. J. , Magazu, J. P., and Boeri, R. L. 1996.
Acute Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] to the Daphnid, *Daphnia magna*. Unpublished Report by T. R. Wilbury Laboratories, Inc. Conducted for Chevron Research and Technology Company. IA: Reliable without restriction; OECD guideline study.

Japanese Environmental Agency. 1992. Investigation of the Ecotoxicological Effects of OECD High Production Volume Chemicals [*Daphnia* sp., Acute Immobilisation Test and Reproduction Test on 1,4-diethylbenzene].
4B: Not assignable; only secondary literature.

Other

Last changed:
Remarks:

September 4, 2001

TOXICITY TO AQUATIC PLANTS (A)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:
Remarks:

Method

Method/guideline followed: OECD Method No. 203
Test type: Static
GLP: Yes
Year: 1995
Analytical procedures: None
Species/Strain: *Selenastrum capricornutum*
Test details: Nominal concentrations were 0, 7, 13, 25, 50, and 100 mg/l.

Exposure period: 96 hours
Analytical monitoring: None
Statistical methods: The EC 10, EC50, and EC90 values were calculated by the probit method, when possible, or the EC50 value was calculated using the binomial method. A parametric one-way analysis of variance (ANOVA) was used to determine the no observed effect concentrations (NOECs) at 72 and 96 hours.

Remarks: Algae used for the test (*Selenastrum capricornutum* UTEX 1648) was from a culture originally procured from the Culture Collection of Algae at the University of Texas at Austin. The culture was transferred to sterile enriched media identical to media used for this test and maintained at test conditions for at least 14 days before the definitive test. The inoculum used to initiate the test was 8 days old. The pH of the test media was 7.5, and had <10 mg/liter total suspended solids and the beginning of the test and 29 mg/liter suspended solids at the end of the test. Algae was distributed among three replicates of the treatment and control at the rate of 10,000 cells/ml. The test was performed in 250 ml glass erlenmeyer flasks that contained 100 ml of test solution. Test vessels were arranged on a rotary shaker adjusted to 100 rpm in an incubator during the test. These vessels were kept at 24 (±1.0)°C. The lighting was maintained by cool-white fluorescent light on a 24-hour daylight photoperiod, providing a light intensity of 350-360 footcandles.

Results

Nominal concentration (mg/l): 0, 7, 13, 25, 50, and 100
Measured concentration (mg/l): not determined
Unit: mg/l

Growth Rate	
EC ₅₀ (72 and 96 hour):	= 63 and 66 mg/l
NOEC (72 and 96 hour):	= 25 mg/l
Cell Density	
EC ₅₀ (72 and 96 hour):	= 41 and 47 mg/l
NOEC (72 and 96 hour):	= 13 and 25 mg/l
Statistical results:	
Remarks:	Insoluble material was noted on the surface of the 25 and 50 mg/liter media at 0, 24, and 48 hours and on the surface of the 100 mg/liter media throughout the test. The algal population grew well during the test, resulting in an average of 1,2 15,000 cells per ml in the control after 96 hours. No effects on size differences, unusual cell shapes, colors, flocculations, adherence of cells to test containers, or aggregation of cells were noted.
Conclusions	The acute toxicity to aquatic plants has been adequately characterized by this study.
Data Quality	
Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; OECD guideline study.
References	Ward, T. J. , Magazu, J. P., and Boeri, R. L. 1996. Acute Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] to the Freshwater Alga, <i>Selenastrum capricornutum</i> . Unpublished Report by T. R. Wilbury Laboratories, Inc. Conducted for Chevron Research and Technology Company.
Other Available Reports	Tucker, M. W., Adams, W. J., and Kimerle, R. A. 1987. Acute Toxicity of MCS 23 13 (Terminol LT) to the Freshwater Green Alga, <i>Selenastrum capricornutum</i> . Monsanto Environmental Sciences Center Report No. ESC-EAG-87-100. 2C: Reliable with restrictions; comparable to guideline study with acceptable restrictions. Japanese Environmental Agency. 1992. Investigation of the Ecotoxicological Effects of OECD High Production Volume Chemicals [The Algal Growth Inhibition Test on 1,4-diethylbenzene]. 4B: Not assignable; only secondary literature.
Other	
Last changed:	September 4, 2001
Remarks:	

TOXICITY TO AQUATIC PLANTS (B)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-1 7-4)
Purity:
Remarks:

Method

Method/guideline followed: EPA Guidelines
Test type: Static
GLP: Yes
Year: 1987
Analytical procedures: None
Species/Strain: *Selenastrum capricornutum*
Test details: Nominal concentrations were 0, 1.24, 2.5 l, 10.03, and 20.06 mg/l.

Exposure period: 96 hours
Analytical monitoring: None
Statistical methods: Not stated
Remarks: Algae used for the test (*Selenastrum capricornutum* Printz) was obtained from the University of Texas Starr Collection and has been maintained in the Monsanto Environmental Sciences Center laboratory for at least six months. The inoculum used to initiate the test was 6 days old and The pH of the test media was 7.3 to 7.4. Algae was distributed among the treatment and control at the rate of 10.000 cells/ml. Test solutions were diluted in dimethylformamide, with a final concentration in the test system of 100 µl/liter. The test was performed in 125 ml glass erlenmeyer flasks that contained 50 ml of test solution. Test vessels were arranged on a rotary shaker adjusted to 100 t-pm in an incubator during the test. These vessels were kept at 25 (±1 .0)°C. The lighting was maintained by cool-white fluorescent light, providing a light intensity of 400 ± 10% foot-candles.

Results

Nominal concentration (mg/l): 0, 1.24, 2.51, 5.01, and 10.03 mg/l
Measured concentration (mg/l): not determined
Unit: mg/l
Reduced biomass
EC₅₀ (96 hour): = >20.06 mg/l
NOEC (96 hour): =

Statistical results:
Remarks:

Insoluble material was noted on the surface of the 25 and 50 mg/liter media at 0, 24, and 48 hours and on the surface of the 100 mg/liter media throughout the test. The algal population grew well during the test,

resulting in an average of 4,300,000 cells per ml in the control after 96 hours. Biomass production was measured by gravimetric determination of the dry weight of the algae solution.

Conclusions

The acute toxicity to aquatic plants has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):
Remarks:

2c
Reliable with restrictions; comparable to guideline study with acceptable restrictions.

References

Tucker, M. W., Adams, W. J., and Kimerle, R. A. 1987. Acute Toxicity of MCS 23 13 (Terminol LT) to the Freshwater Green Alga, *Selenastrum capricornutum*. Monsanto Environmental Sciences Center Report No. ESC-EAG-87-100.

Other Available Reports

Ward, T. J. , Magazu, J. P., and Boeri, R. L. 1996. Acute Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] to the Freshwater Alga, *Selenastrum capricornutum*. Unpublished Report by T. R. Wilbury Laboratories, Inc. Conducted for Chevron Research and Technology Company.
IA: Reliable without restriction; OECD guideline study.

Japanese Environmental Agency. 1992. Investigation of the Ecotoxicological Effects of OECD High Production Volume Chemicals [The Algal Growth Inhibition Test on 1,4-diethylbenzene].
4B: Not assignable; only secondary literature.

Other

Last changed:
Remarks:

September 4, 2001

ACUTE ORAL TOXICITY (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	FIFRA/TSCA guidelines
Type:	LD ₅₀
GLP:	Not stated
Year:	1987
Species/Strain:	Sprague-Dawley rats
Sex :	male and female
No. of animals per sex per dose:	5
Vehicle:	None
Route of administration:	Oral/gastric intubation
Remarks:	At the start of experiment, animals were about 9 to 12 weeks of age with a weight of 292 to 355 grams for males, and 224 to 253 grams for females. Room temperature was 67 to 76°F, and relative humidity was between 30 to 70% during the study. Animals were observed for 14 days postdose.

Results

LD ₅₀ value:	= 2050 mg/kg (confidence range 1770 to 2330 mg/kg)
Number of deaths:	1700 mg/kg = 2 dead days 3 and 6 2500 mg/kg = 9 dead days 1-3 3500 mg/kg = 10 dead days 1-5 5000 mg/kg = 10 dead days 1-3
Remarks:	A variety of abnormal signs occurred on the day of dosing. Several animals exhibited hypoactivity, red nasal discharge, urinary staining, partially closed eyes, prostration, and decreased food consumption. Signs seen in a few animals (in most groups) included ataxia, tremors, clear nasal and oral discharges, wet rales, soft stool, fecal staining and abdominal griping. A few animals exhibited blue pigmentation and hypothermia on the day of dosing; by day 2 or 3, a majority of the survivors were exhibiting these signs. Postmortem examinations of animals which were found dead revealed a variety of changes, primarily blue pigmentation of all/most soft tissues and/or blue fluid in the gastrointestinal tract and urinary bladder. Other changes seen in most animals which were found dead included changes in the stomach, intestine and urinary bladder which were suggestive of an irritant and/or corrosive effect

Conclusions

Data Quality

Reliability (Klimisch):

Remarks:

1B

Reliable without restrictions; comparable to guideline study.

Reference

Biodynamics Inc. 1987. Acute Oral Toxicity Study in Rats. Unpublished report 4086-87. Submitted to EPA by Monsanto Inc., as EPA Doc. No. 8EHQ-0892-8828

Other Available Reports

Chevron. 199 1. The Acute Oral Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] in Male and Female Rats. Unpublished Report No. 90-1 8.

1 A: Reliable without restrictions: guideline study.

MHW, Japan. 1993. Single Oral Toxicity Test of 1,4-Diethylbenzene in Rats. Unpublished Report for OECD-SIDS program.

4B: Not assignable; only secondary literature.

Other

Last changed:

September 4, 200 1

Remarks:

ACUTE ORAL TOXICITY (B)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity: Not stated
Remarks:

Method

Method/guideline followed: FIFRA/TSCA guidelines
Type: LD₅₀
GLP: Yes
Year: 1990-1991
Species/Strain: Sprague-Dawley rats
Sex: male and female
No. of animals per sex per dose: 5
Vehicle: Not stated
Route of administration: Oral/gastric intubation
Remarks: At start of the experiment, males were 74 days old with a weight of 225 to 340 grams, and females were 81 days old with a weight of 170 to 254 grams. Room temperature was 17 - 23°C, and relative humidity was between 45 - 65% during the study. Animals were observed for 14 days postdose.

Results

LD₅₀ value: = 6900 mg/kg for males; and 4700 mg/kg for females (95% confidence limits of 3800 to 12100 g/kg)
Number of deaths:
3400 mg/kg = males and females: no deaths
4300 mg/kg = 1 dead on day 4 (males); 2 dead on day 3 (females)
5000 mg/kg = 1 dead on day 1 (males); 3 dead on days 2-3 (females)
7700 mg/kg = 3 dead on days 3-6 (males); 5 dead on days 2-4 (females)
Remarks: Treated animals displayed similar patterns of toxicity that usually began with some variety of motor dysfunction (awkward gait, splayed fore- and hindlimbs) beginning approximately 6.5 hours after dosing. Tremors were also observed in some treated females of the 4300, 5000, and 7700 mg/kg dose groups, beginning 6 hours post-dosing. Cyanosis was observed in one treated male treated with 5000 mg/kg, 6.5 hours post-dosing. At Day 1, symptomology consistent with generalized central nervous system depression was observed in all treated animals. Several treated animals were found either comatose or unable to maintain normal posture. All treated animals exhibited reductions in spontaneous motor activity, abnormal righting reflexes, and decreases in responsiveness to extraneous sensory stimuli. Green urine was also observed on Day 1 in all dose groups.

Other signs of toxicity included but were not limited to reductions in the rate and depth of breathing, red nasal discharge, ocular and anogenital discharge, diarrhea, reduced pupil response, mydriasis, lacrimation, and partial palpebral closure. On Day 2, cyanosis developed within all treatment groups with the exception of females treated with 3400 and 4300 mg/kg. No treatment-related signs of toxicity were observed after Day 8 in surviving animals. At necropsy, dark fluid was found in the bladders of some animals treated with >3400 mg/kg. The gross appearance of these bladders were normal.

Conclusions

Data Quality

Reliability (Klimisch):
Remarks :

IA
Reliable without restrictions; guideline study.

Reference

Chevron. 1991. The Acute Oral Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] in Male and Female Rats. Unpublished Report No. 90- 18.

Other Available Reports

Biodynamics Inc. 1987. Acute Oral Toxicity Study in Rats. Unpublished report BD-87-093. Submitted to EPA by Monsanto Inc., as EPA Doc.No. 8EHQ-0892-8828 1B: Reliable without restrictions; comparable to guideline study.

MHW, Japan. 1993. Single Oral Toxicity Test of 1,4-Diethylbenzene in Rats. Unpublished Report for OECD-SIDS program.
4B: Not assignable; only secondary literature.

Other

Last changed:
Remarks:

September 4,200 1

ACUTE DERMAL TOXICITY (A)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-1 7-4)
Purity: Not stated
Remarks:

Method

Method/guideline followed: FIFRA/TSCA guidelines
Type: LD₅₀
GLP: Yes
Year: 1987
Species/Strain: New Zealand White rabbits
Sex: male and female
No. of animals per sex per dose: 5
Vehicle: Not stated
Route of administration: Dermal
Remarks: At start of the experiment, animals were at least 8 weeks old. The males weighed between 2.3-2.6 kg, and the females weighed between 2.6-2.7 kg. Room temperature was 60-70°F, and relative humidity was between 30-70% during the study. Animals were observed for 14 days postdose.

Results

LD₅₀ value: = >5000 mg/kg

Remarks: All animals exhibited body weight losses or no weight change at Day 7, but most gained weight between Days 7 and 14. Except for fissuring exhibited at a small portion of the dose site, in one animal, no severe dermal effects were seen. Decreased food consumption was exhibited by all ten animals on the day after dosing; by four animals on Day 4; and by one animal on Day 10.

Conclusions

Data Quality

Reliability (Klimisch): 1A
Remarks: Reliable without restrictions; guideline study.

Reference

Biodynamics Inc. 1987. Acute Dermal Toxicity Study in Rabbits. Unpublished report 40X7-87. Submitted to EPA by Monsanto Inc., as EPA Doc. No. 8EHQ-0892-8828

Other Available Reports

Chevron, 199 1. The acute dermal toxicity of polyethylbenzene [Mixed Diethylbenzenes] (MF-335) in rats. Unpublished Report. Study Number CEHC 3172, Chevron Environmental Health Center, Richmond, CA.

Other

Last changed:

September 13, 200 I

Remarks:

ACUTE DERMAL TOXICITY (B)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-1 7-4)
Purity: Not stated
Remarks:

Method

Method/guideline followed: FIFRA/TSCA guidelines
Type: LD₅₀
GLP: Yes
Year: 1990
Species/Strain: Sprague-Dawley rats
Sex: male and female
No. of animals per sex per dose: 5
Vehicle: None
Route of administration: Dermal
Remarks: At start of the experiment, males were 71 weeks old and the females were 77 weeks old. The males weighed between 346 and 380 grams, and the females weighed between 228 and 266 grams. Room temperature was 20-22°C, and relative humidity was between 34-56% during the study. Animals were observed for 14 days postdose.

Results

LD₅₀ value: = >2000 mg/kg

Remarks: Compound-related signs of toxicity were limited to a yellow anogenital discharge in a single treated male. Skin irritation consisting of red, swollen and scabbed skin was more persistent and severe in treated animals than in controls. A significant decrease in mean body weight gain was observed in treated males on Days 0-2.

Conclusions

Data Quality

Reliability (Klimisch): 1A
Remarks: Reliable without restrictions; guideline study.

Reference

Chevron, 199 1. The acute dermal toxicity of polyethylbenzene [Mixed Diethylbenzenes] (MF-335) in rats. Unpublished Report. Study Number CEHC 3 172, Chevron Environmental Health Center, Richmond, CA.

Other Available Reports

Biodynamics Inc. 1987. Acute Dermal Toxicity Study in Rabbits. Unpublished report 4087-87. Submitted to EPA by Monsanto Inc., as EPA Doc. No. 8EHQ-0892-8828

Other

Last changed: September 13, 200 1
Remarks:

REPEATED DOSE TOXICITY (A)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity: Not stated
Remarks:

Method

Method/guideline followed: EPA Guidelines
Test type: Inhalation
GLP: Yes
Year: 1991-1992
Species: Rat
Strain: Sprague-Dawley
Route of administration: Inhalation
Duration of test: 3 months
Doses/concentration levels: 200,600, and 1200 mg/m³
Sex: Male and female
Exposure period: 10 weeks (mixture) and 8 weeks (isomers)
Frequency of treatment: 6 hours/day, five days/week
Control group and treatment: Concurrent
Postexposure observation period: None
Statistical methods: Dunnett's Multiple Comparison Test (two-tailed) for inlife body weights. Hematology data, clinical chemistry data, terminal body weights, absolute organ weights and organ/body weight ratios were evaluated by decision-tree statistical analyses which, depending on the results of tests for normality and homogeneity of variances (Bartlett's Test), utilized either parametric (Dunnett's Test and Linear Regression) or non-parametric (Kruskal-Wallis, Jonckheere's and/or Mann-Whitney Tests) routines to detect differences and analyze for trends. Fisher's Exact Test (one-tailed) was used for incidence of microscopic lesions
Remarks: There were 10 rats/group. The mean analytical concentrations were 0, 190, 610, and 1400 mg/m³. Each exposure level was sampled four times daily, and the control chamber was sampled weekly, for test material concentration. Animals were checked twice daily for mortality and following each exposure for gross signs of toxicity. During exposure, visible animals were observed for signs of toxicity. Body weights and clinical observations were performed weekly. Ophthalmic examinations were performed pretest on all animals and just prior to termination on control and high-exposure level animals. Clinicopathologic examinations were performed at termination. All animals were given a gross necropsy. All retained tissues from the control and high-exposure level groups were examined microscopically.

Results

NOAEL:

Toxic response/effects:

190 mg/m³

Decreased mean body weights in the high-dose group animals throughout the study. There were no abnormal clinical observations which were considered to be treatment-related. There were no ocular abnormalities attributed to administration of the test material. Treatment-related changes in hematologic parameters included moderate decreases in total white cell and lymphocyte counts in the mid- and high-exposure level males. Abnormal sera color (blue or blue-gray) was observed in high-exposure level animals of both sexes. Treatment-related changes in serum chemistry parameters included decreases in ALT, AST, and CPK in high-exposure level females and increases in potassium in high-level males and phosphorus in males from the high-exposure group and females from the mid- and high-exposure groups. An abnormal blue-gray color was observed in most tissues from all but one high-exposure animal. At the mid-exposure level, the same color was observed in brains of eight males and all females and in the urinary bladders of five females and one male. This abnormal color probably resulted from the presence of the parent chemical or a metabolite in these tissues. However, there was no other gross or microscopic changes attributed to the test material.

Statistical results:

Remarks:

Conclusions

Repeated exposures to Mixed Diethylbenzenes (CAS No. 25340-17-4) did not result in any target organ toxicity. This endpoint has been adequately covered.

Data Quality

Reliability (Klimisch):

Remarks:

1A

Reliable without restriction: EPA Guideline study.

Reference

Kaempfe, T. A. and Thake, D. C. 1993. Three-Month Inhalation Study of MCS 23 13 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570.

Other Available Reports

Gagnaire, F., Marignac, B., and de Ceaurriz, J. (1990) Diethylbenzene-induced sensorimotor neuropathy in rats. J. Applied Toxicology 10(2): 105-112.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Ensminger A., Marignac, B., and De Ceuriz (1991) Possible involvement of 1,2-diacetylbenzene in diethylbenzene-induced neuropathy in rats. J. Appl. Toxicology 11(4) 261-268.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., Marignac, B., Bonnet, P., and DeCeuriz, J. (1992) Diethylbenzene inhalation-induced electrophysiological deficits in peripheral nerves and changes in brainstem auditory evoked potential in rats. J. Applied Toxicology 12(5): 335-342.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., and De Ceuriz, J. (1992) Alteration of brainstem auditory evoked potentials in diethylbenzene and diacetylbenzene-treated rats. J. Applied Toxicology 12(5): 343-350.
3D: Not reliable. Relevant methodological deficiencies.

MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.
4A: Not assignable; only short abstract available.

Other

Last changed:
Remark:

September 4, 2001

REPEATED DOSE TOXICITY (B)

Test Substance

Identity: Diethylbenzene (DEB) mixture (approx. 7% 1,2-diethylbenzene, 58% 1,3-diethylbenzene 35% 1,4-diethylbenzene) or individual diethylbenzene isomers

Purity: 95% 1,2-diethylbenzene, 99% 1,3-diethylbenzene, 96% 1,4-diethylbenzene

Remarks:

Method

Method/guideline followed: Not stated

Test type: Oral

GLP: No

Year:

Species: Rat

Strain: Sprague-Dawley

Route of administration: Oral gavage

Duration of test: 8 or 10 weeks

Doses/concentration levels: 500 or 750 mg/kg (in olive oil) for DEB mixture; 100 mg/kg for 1,2-diethylbenzene; and 500 mg/kg for 1,3- and 1,4-diethylbenzene

Sex: No specified

Exposure period: 10 weeks (mixture) and 8 weeks (isomers)

Frequency of treatment: 5 days/week (mixture and 1,3- and 1,4-diethylbenzene isomers); 4 days/week (1,2-diethylbenzene)

Control group and treatment: Concurrent, given olive oil vehicle

Postexposure observation period: 8 weeks (isomer study only)

Statistical methods: Differences in mean body weight, motor and sensory conduction velocities, and amplitude of the sensory action potential between experimental and control groups were analyzed using Student's t-test for independent data. Mean electrophysiological deficits in the tail nerve were also analyzed, as a function of the length of treatment, by least-squares regression.

Remarks: There were 12 rats/group. Rats were subjected to neurophysiological measurements every week during the treatment period. The survivors were kept for observation and neurophysiological measurements during the post-exposure period. The motor conduction velocity (MCV) and sensory conduction velocity (SCV) of the tail nerve and the amplitude of the sensory action potential (ASAP) were adopted as parameters for testing peripheral nerve function in rats.

Results

LOAEL: 500 mg/kg (DEB mixture); and 100 mg/kg (1,2-diethylbenzene)

NOAEL: 500 mg/kg (1,3- and 1,4-diethylbenzene)

Toxic response/effects: Described below

Statistical results:
Remarks:

Described below

Diethylbenzene mixture

Rats given diethylbenzene (DEB) mixture with either 500 or 750 mg/kg exhibited a blue discoloration of the skin and urine as soon as the 3rd day of treatment. A significant reduction in weight gain was observed from the first week of treatment in the group treated with 750 mg/kg. Two animals died in the 750 mg/kg dose group during the first week of treatment. Two rats died in the 500 mg/kg group during the 4th and 7th weeks of treatment. No animals died in the control group. Rats in the DEB-dosed groups developed severe weakness in hind limbs and disturbances in gait from the 4th week of treatment. This weakness got worse in the following weeks, resulting in a complete paralysis of the hind limbs for some rats. There was a time-dependent decrease in MCV, SCV, and ASAP.

Diethylbenzene isomers

Rats given 1,2-diethylbenzene developed the same symptoms (decreased body weight, blue discoloration of skin and urine, weakness of hind limbs, paralysis) as those described for the diethylbenzene mixture.

One rat died in the first week of treatment and another died in the 5th week of treatment. 1,3- and 1,4-Diethylbenzene-treated rats did not display any signs of neurotoxicity or any other signs of systemic toxicity. During the recovery period, the 1,2-diethylbenzene treated rats regained weight, became more mobile but presented trailing hind limbs, when attempting to walk. On the 4th week of recovery, all animals treated with 1,2-diethylbenzene succeeded in standing up. A time-dependent decrease in MCV, SCV, and ASAP was observed in animals dosed with 1,2-diethylbenzene, but not with 1,3- or 1,4-diethylbenzene.

Conclusions

Oral exposure to diethylbenzene mixture and 1,2-diethylbenzene produced adverse effects on the peripheral nervous system, whereas 1,3- and 1,4-diethylbenzene did not.

Data Quality

Reliability (Klimisch):
Remarks:

3 D
Not reliable. Relevant methodological deficiencies.

Reference

Gagnaire, F., Marignac, B., and de Ceuriz, J. (1990) Diethylbenzene-induced sensorimotor neuropathy in rats. J. Applied Toxicology 10(2): 105-112.

Other Available Reports

Gagnaire, F., Ensminger A., Marignac, B., and De Ceuriz (1991) Possible involvement of 1,2-

diacetylbenzene in diethylbenzene-induced neuropathy in rats. J. Appl. Toxicology 11(4) 261-268.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., Marignac, B., Bonnet, P., and DeCeuriz, J. (1992) Diethylbenzene inhalation-induced electrophysiological deficits in peripheral nerves and changes in brainstem auditory evoked potential in rats. J. Applied Toxicology 12(5): 335-342.

3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., and De Ceuriz, J. (1992) Alteration of brainstem auditory evoked potentials in diethylbenzene and diacetylbenzene-treated rats. J. Applied Toxicology 12(5): 343-350.

3D: Not reliable. Relevant methodological deficiencies.

MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.

4A: Not assignable; only short abstract available.

Other

Last changed:

September 13, 2001

Remark:

REPEATED DOSE TOXICITY (C)

Test Substance

Identity: Diethylbenzene (DEB) mixture (approx. 6% 1,2-diethylbenzene, 66% 1,3-diethylbenzene 28% 1,4-diethylbenzene)

Purity: Not stated

Remarks:

Method

Method/guideline followed: Not stated

Test type: Inhalation

GLP: No

Year:

Species: Rat

Strain: Sprague-Dawley

Route of administration: Inhalation

Duration of test: 18 weeks

Doses/concentration levels: 500,700, and 900 ppm in experiment A; 600 and 800 ppm in experiment B

Exposure period: 18 weeks

Frequency of treatment: 6 hours/day, 5 days/week

Control group and treatment: Concurrent

Postexposure observation period: 6 or 7 weeks

Statistical methods: Statistical differences among groups were evaluated for each variable on each session by one-way analysis of variance. *Post hoc* individual mean comparisons were made with Duncan's multiple range test.

Remarks: There were 12 rats/group in experiment A and 15 rats/group in experiment B. Rats were subjected to neurophysiological measurements every two weeks during the entire exposure period in experiment A, and every two weeks for the first 9 weeks of exposure in experiment B and then every three weeks thereafter. The survivors were kept for observation and neurophysiological measurements during the post-exposure period. The motor conduction velocity (MCV) and sensory conduction velocity (SCV) of the tail nerve and the amplitude of the sensory action potential (ASAP) were adopted as parameters for testing peripheral nerve function in rats in experiment A. In experiment B, only brainstem auditory evoked potential (BAEP) was measured.

Results

LOAEL: 500 ppm

Toxic response/effects: Described below

Statistical results: Described below

Remarks: Experiment A

Exposure to DEB reduced weight gain from the first week of exposure in each group. There was no mortality in the control, 500 or 700 ppm exposed groups. In the 900 ppm group, one animal was euthanized on the fifth week of exposure due to an abscess at the neck. The animals of the 700 and 900 ppm exposed groups were prostrate during the exposure period but recovered a few hours after the end of the exposure period. Rats in the all DEB-exposed groups developed blue skin discoloration after three weeks of exposure. No animal in any group exhibited disturbances in gait or other signs of neurotoxicity. There was a time- and concentration-dependent decrease in MCV, SCV, and ASAP, which did not completely reversed during the 6-week recovery period.

Experiment B

Weight gain was reduced in the DEB-exposed groups. From the third week of exposure, the DEB-exposed groups exhibited the blue skin discoloration. At the end of the exposure period, some animals exhibited disturbances in gait and one animal in the 800 ppm group had partial paralysis in the hindlimbs. Two animals died in the 800 ppm group during the exposure period, and 8 animals/group had to be euthanized during the study because they lost their head plugs during the recording sessions. There was a time- and concentration dependent increase in both the peak latencies of all BAEP components and the inter-peak (I-V) differences. Partial, but not complete reversal, occurred during the 7-week recovery period.

Conclusions

Inhalation exposure to diethylbenzene mixtures appear to have adverse effects on the peripheral and central nervous system. There seems to be, however, some inconsistencies between the two experiments with regards to the clinical signs of peripheral nervous system damage. The authors proposed that this difference may be due to the age of the rats used in these two experiments, 9-and 19-week old, respectively.

Data Quality

Reliability (Klimisch):
Remarks:

3 D
Not reliable. Relevant methodological deficiencies.

Reference

Gagnaire, F., Becker, M. N., Marignac, B., Bonnet, P., and De Ceaurriz, J. (1992) Diethylbenzene inhalation-induced electrophysiological deficits in peripheral nerves and changes in brainstem auditory evoked

potentials in rats. J. Applied Toxicology 12(5): 335-342.

Other Available Reports

Kaempfe, T. A. and Thake, D. C. Three-Month Inhalation Study of MCS 23 13 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570.

Gagnaire, F., Marignac, B., and de Ceaurriz, J. (1990) Diethylbenzene-induced sensorimotor neuropathy in rats. J. Applied Toxicology 10(2) 105-112. 3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Ensminger A., Marignac, B., and De Ceaurriz (1991) Possible involvement of 1,2-diacetylbenzene in diethylbenzene-induced neuropathy in rats. J. Appl. Toxicology 11(4) 261-268. 3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., and De Ceaurriz, J. (1992) Alteration of brainstem auditory evoked potentials in diethylbenzene and diacetylbenzene-treated rats. J. Applied Toxicology 12(5): 343-350. 3D: Not reliable. Relevant methodological deficiencies.

MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program. 4A: Not assignable; only short abstract available.

Other

Last changed:
Remarks:

September 4, 2001

GENETIC TOXICITY *IN VITRO* (A)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340- 17-4)
Purity:
Remarks:

Method

Method/guideline followed: OECD Method No. 47 1
Type : *Salmonella* reverse mutation assay
System of testing: Bacterial
GLP: Yes
Year: 1990
Species/Strain: *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 with S-9 activation and without S-9 activation
Metabolic activation: Liver S-9 fraction from Aroclor 1254 pretreated (injected, ip) male Sprague-Dawley rats.
Concentrations tested: 0.003, 0.01, 0.033, 0.1, 0.333, 1.0, 3.33, 10.0 mg/plate
Statistical methods: Not stated
Remarks: Positive (2-aminoanthracene, 2-nitrofluorene, and sodium azide) and negative controls were included. Eight doses in addition to the concurrent solvent and positive controls were tested on each strain in the presence of S-9 mix or buffer. Three plates were used, and the results were confirmed in an independent experiment.

Results

Result: Negative
Cytotoxic concentration: > 1 mg/plate
Genotoxic effects: Negative
Statistical results: Statistically significant increases in the number of revertants were observed for TA98 and TA 100 in the presence of metabolic activation. These responses were not reproducible and were, therefore, not considered to be biologically significant.

Remarks:

Conclusions

Mixed diethylbenzenes (25340- 17-4) did not cause mutations to *S. typhimurium* in this *in vitro* genetic toxicity test. The bacterial mutation potential of mixed diethylbenzenes (25340-17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):

1A

Remarks:

Reliable without restriction; OECD guideline study.

Reference

Chevron. 199 1. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.

Other Available Reports

Stankowski, L. F. **1988** Ames/*Salmonella* Plate Incorporation Assay. Pharmakon Research International, Inc. Study No. 301-MO-002-88. Conducted for Monsanto Company.

1A: Reliable without restriction; EPA guideline study.

Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 23 13 (mixed diethylbenzene stream, CAS No. 25340-17-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002.

IA: Reliable without restriction; EPA guideline study.

MWH, Japan. 1993. Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program.

4B: Not assignable; only secondary literature.

Other

Last changed:

September 4, 200 1

Remarks:

GENETIC TOXICITY *IN VITRO*(B)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity: Not specified
Remarks:

Method

Method/guideline followed: OECD Method No. 47 1
Type: *E. coli*
System of testing: Bacterial
GLP: Yes
Year: 1990
Species/Strain: *E. coli* WP2 uvrA with S-9 activation and without S-9 activation
Metabolic activation: Liver S-9 fraction from Aroclor 1254 pretreated (injected, ip) male Sprague-Dawley rats.
Concentrations tested: 0.003, 0.01, 0.033, 0.1, 0.33, 1.0, 3.33, 10.0 mg/plate
Statistical methods: Not stated.
Remarks: Positive (2-aminoanthracene and ICR- 191) and negative controls were included. Eight doses in addition to the concurrent solvent and positive controls were tested in the presence of S-9 mix or buffer. Three plates were used, and results were confirmed in an independent experiment.

Results

Result: Negative
Cytotoxic concentration: > 1 mg/plate
Genotoxic effects: Negative
Statistical results:
Remarks: Cytotoxicity was also observed in WP2 uvrA without S-9 at dose levels of 0.1 and 0.33 mg/plate in a single experiment. Since WP2 uvrA is generally more resistant to toxicity than the *Salmonella* strains (which tested in the same experiment; see 5.5A), and the toxicity was observed also in the positive controls where it was not expected, it was concluded that the cytotoxic response in WP2 uvrA without activation at 0.1 and 0.33 mg/plate was probably not treatment-related.

Conclusions

Mixed diethylbenzenes (25340-1 7-4) did not cause mutations to *E. coli* in this *in vitro* genetic toxicity test. The bacterial mutation potential of mixed diethylbenzenes (25340-17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch): 1A
Remarks: Reliable without restriction; OECD guideline study.

Reference

Chevron. 1991. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.

Other Available Reports

Stankowski, L. F. 1988 Ames/*Salmonella* Plate Incorporation Assay. Pharnakon Research International, Inc. Study No. 301 -MO-002-88. Conducted for Monsanto Company.

1A: Reliable without restriction; EPA guideline study.

Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 23 13 (mixed diethylbenzene stream, CAS No. 25340-1 7-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002.

1A: Reliable without restriction; EPA guideline study.

MWH, Japan. 1993. Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program.

4B: Not assignable; only secondary literature.

Other

Last changed:

September 4, 2001

Remarks:

GENETIC TOXICITY IN *VITRO* (C)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:
Remarks:

Method

Method/guideline followed: EPA Guidelines
Type: *Salmonella* reverse mutation assay
System of testing: Bacterial
GLP: Yes
Year: 1988
Species/Strain: *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 with S-9 activation and without S-9 activation
Metabolic activation: Liver S-9 fraction from Aroclor 1254 pretreated male Sprague-Dawley rats.
Concentrations tested: 0.00167, 0.005, 0.0167, 0.05, 0.167, 0.5 mg/plate
Statistical methods: Not stated
Remarks: Positive (2-aminoacridine, 2-nitrofluorene, 2-antramine and sodium azide) and negative controls were included. Six doses in addition to the concurrent solvent and positive controls were tested on each strain in the presence of S-9 mix or buffer. Three plates were used, and the results were confirmed in an independent experiment.

Results

Result: Negative
Cytotoxic concentration: > 0.05 mg/plate
Genotoxic effects: Negative
Statistical results:
Remarks:

Conclusions

Mixed diethylbenzenes (25340-17-4) did not cause mutations to *S. typhimurium* in this *in vitro* genetic toxicity test. The bacterial mutation potential of mixed diethylbenzenes (25340-17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):

1A

Remarks:

Reliable without restriction; guideline study.

Reference

Stankowski, L. F. 1988 Ames/Salmonella Plate Incorporation Assay. Pharmakon Research International, Inc. Study No. 30 1 -MO-002-88. Conducted for Monsanto Company.

Other Available Reports

Chevron. 199 1. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.

1A: Reliable without restriction; OECD guideline study.

Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 23 13 (mixed diethylbenzene stream, CAS No. 25340- 17-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002.

1A: Reliable without restriction; EPA guideline study.

MWH, Japan. 1993. Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program.

4B: Not assignable; only secondary literature.

Other

Last changed:

September 4, 200 1

Remarks:

GENETIC TOXICITY IN *VITRO*(D)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340- 17-4)
Purity:
Remarks:

Method

Method/guideline followed: EPA Guidelines
Type: Chromosomal aberration assay
System of testing: mammalian cells
GLP: Yes
Year: 1988
Species/Strain: Chinese Hamster Ovary cells with and without S-9 activation
Metabolic activation: Liver S-9 fraction from Aroclor 1254 pretreated Sprague-Dawley rats.
Concentrations tested: 25, 40, 50, 60, and 75 ug/ml
Statistical methods: Chi-square analysis was used to analyze the number of cells with structural aberrations. Dunnett's t-test was used to analyze structural aberrations per cell.
Remarks: Positive (methyl methane sulfonate and cyclophosphamide) and negative controls were included. Five doses in addition to the concurrent solvent and positive controls were tested in the presence of S-9 mix or buffer. Duplicate samples per treatment condition were used and the cells were harvested at 12 and 24 hours after initiation of treatment.

Results

Cytotoxic concentration: > 50 ug/ml
Genotoxic effects: Negative
Statistical results:
Remarks:

Conclusions

Mixed diethylbenzenes (25340-17-4) did not cause any statistically significant increase in the number of cells with structural aberrations or in the average structural aberrations per cell. The clastogenic potential of mixed diethylbenzenes (25340- 17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):

Remarks:

IA

Reliable without restriction: EPA guideline study.

Reference

Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 23 13 (mixed diethylbenzene stream, CAS No. 25340-1 7-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002.

Other Available Reports

Chevron. 199 1. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.

1A: Reliable without restriction; OECD guideline study.

Stankowski, L. F. **1988** Ames/*Salmonella* Plate Incorporation Assay. Pharmakon Research International, Inc. Study No. 301-MO-002-88. Conducted for Monsanto Company.

1A: Reliable without restriction; EPA guideline study.

MWH, Japan. 1993, Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program.

4B: Not assignable; only secondary literature.

Other

Last changed:

Remarks:

September 4,200 1

GENETIC TOXICITY IN *VIVO*

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity: Not specified
Remarks:

Method

Method/guideline followed: OECD Method No. 474
Type: Micronuclei formation in bone marrow erythrocytes
GLP: Yes
Year: 1990
Species: Mouse
Strain: CD-1
Sex: Male and female
Route of administration: Intraperitoneal
Doses/concentration levels: 1000, 2000, and 4000 mg/kg (diluted with peanut oil)
Exposure period: Single dose
Statistical methods:
Remarks: Vehicle and positive controls were dosed intraperitoneally with peanut oil and cyclophosphamide, respectively. Number of animals: 1 ♂/sex/group, except for the positive control group (5/sex). Bone marrow smears, 5 animals/sex/dose, were made at approximately 24, 48, and 72 hours post-dosing.

Results

Cytotoxicity: Cytotoxicity was noted in females dosed with 4000 mg/kg and sampled at 48 hours.

Genotoxic effects: No treatment-related effect on increased micronucleated polychromatic erythrocytes in either sex.

NOEC or LOAEC: 1000 mg/kg

Statistical results: No statistically significant differences between mixed diethylbenzene-exposed animals and controls.

Remarks: Evidence of toxicity was found at ≥ 2000 mg/kg in both sexes. Clinical signs of toxicity observed were decreased motor activity, collapse, labored breathing, convulsions, and weakness. In addition, on Day 1, one male at 2000 mg/kg and three males and one female at 4000 mg/kg died before the scheduled sampling time; two moribund females at 4000 mg/kg were euthanized.

Conclusions

Under the conditions of this study, mixed diethylbenzene (25340-17-4) was considered non-genotoxic, since micronuclei were not induced in the bone marrow erythrocytes of mice.

Data Quality

Reliability (Klimisch): 1A
Remarks: Reliability without restriction; OECD guideline study.

References

Chevron. 199 1. Micronucleus Assay in Mouse Bone Marrow Erythrocytes: Polyethylbenzene [Mixed Diethylbenzenes]. Unpublished Report No. 90-24.

Other Available Reports

MHW, Japan. 1993. In Vitro Chromosomal Aberration Test of 1,4-Diethylbenzene on Cultured Chinese Hamster Cells. Unpublished Report for the OECD-SIDS program. 4B: Not assignable; only secondary literature.

Other

Last changed:

September 4,200 I

Remarks:

REPRODUCTIVE TOXICITY (A)

Test Substance

Identity: Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity: Not stated
Remarks:

Method

Method/guideline followed: EPA Guidelines
Test type: Inhalation
GLP: Yes
Year: 1991-1992
Species: Rat
Strain: Sprague-Dawley
Route of administration: Inhalation
Duration of test: 3 months
Doses/concentration levels: 200,600, and 1200 mg/m³
Sex: Male and female
Exposure period: 10 weeks (mixture) and 8 weeks (isomers)
Frequency of treatment: 6 hours/day, five days/week
Control group and treatment: Concurrent
Postexposure observation period: None
Statistical methods: Dunnett's Multiple Comparison Test (two-tailed) for in-life body weights. Absolute organ weights and organ/body weight ratios were evaluated by decision-tree statistical analyses which, depending on the results of tests for normality and homogeneity of variances (Bartlett's Test), utilized either parametric (Dunnett's Test and Linear Regression) or non-parametric (Kruskal-Wallis, Jonckheere's and/or Mann-Whitney Tests) routines to detect differences and analyze for trends. Fisher's Exact Test (one-tailed) was used for incidence of microscopic lesions
Remarks: There were 10 rats/group. The mean analytical concentrations were 0, 190, 610, and 1400 mg/m³. Each exposure level was sampled four times daily, and the control chamber was sampled weekly, for test material concentration. Animals were checked twice daily for mortality and following each exposure for gross signs of toxicity. During exposure, visible animals were observed for signs of toxicity. Body weights and clinical observations were performed weekly. All animals were given a gross necropsy. All retained tissues, including ovaries, pituitary, prostate, seminal vesicles, testes with epididymides, and uterus (corpus and cervix), from the control and high-exposure level groups were examined microscopically.

Results

NOAEL: 190 mg/m³

Toxic response/effects:

Decreased mean body weights in the high-dose group animals throughout the study. There were no abnormal clinical observations which were considered to be treatment-related. An abnormal blue-gray color was observed in most tissues from all but one high-exposure animal. At the mid-exposure level, the same color was observed in brains of eight males and all females and in the urinary bladders of five females and one male. This abnormal color probably resulted from the presence of the parent chemical or a metabolite in these tissues. However, there were no other gross or microscopic changes in the reproductive tissues attributed to the test material.

Statistical results:

Remarks:

Conclusions

Mixed Diethylbenzene Stream (25340-17-4) does not appear to target the reproductive organs in rats.

Data Quality

Reliability (Klimisch):

Remarks:

2c

Reliable with restrictions; comparable to guideline study with acceptable restrictions.

Reference

Kaempfe, T. A. and Thake, D. C. Three-Month Inhalation Study of MCS 23 13 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570.

Other Available Reports

MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.

4A: Not assignable; only short abstract available.

Other

Last changed:

Remark:

September 4, 200 1

REPRODUCTIVE TOXICITY(B)

Test Substance

Identity: 1,4-Diethylbenzene (CAS No. 105-05-5)
Purity: 97.2%
Remarks:

Method

Method/guideline followed: OECD Guideline No. 422
Test type: Inhalation
GLP: Yes
Year: 1993
Species: Rat
Strain: Sprague-Dawley
Route of administration: Oral gavage
Duration of test: Male: 44 days including 14 days before mating
Female: 14 days before mating to lactation day 3
Doses/concentration levels: 30, 150, and 750 mg/kg
Sex: Male and female
Exposure period: Male: 44 days including 14 days before mating
Female: 14 days before mating to lactation day 3
Frequency of treatment: 7 days/week
Control group and treatment: Concurrent
Postexposure observation period: None
Statistical methods: Not stated

Remarks: There were 12 rats/sex/group.

Results

NOAEL: 350 mg/kg/day?
Toxic response/effects: Male and female copulation and fertility indices, pregnancy rates, and implantation sites were comparable among groups. The number of live and dead pups, the number of litters with live offspring, the mean litter size, and the male-to-female ratio were comparable among the groups on lactation day 0. There were no differences in mean pup weights across groups. No differences were found in external observations; and no remarkable findings were observed at necropsy in pups found dead prior to lactation day 4. Duration of gestation was slightly, but statistically significantly, increased in the 750 mg/kg group and there was a statistically significant decrease in pup survival on day 4 in the 750 mg/kg group; however, the investigators did not consider these findings treatment-related.

Statistical results:
Remarks:

Conclusions

1,4-Diethylbenzene (105-05-5) does not appear to be a reproductive toxicant, although a slight effect was observed on duration of gestation.

Data Quality

Reliability (Klimisch):

4A

Remarks:

Not assignable; only short abstract available.

Reference

OECD-SIDS Dossier on 1,4-Diethylbenzene (CAS No. 105-05-5). MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.

Other Available Reports

Kaempfe, T. A. and Thake, D. C. Three-Month Inhalation Study of MCS 23 13 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570.

2C: Reliable with restrictions; comparable to guideline study with acceptable restrictions.

Other

Last changed:

September 4, 200 1

Remark:

DEVELOPMENTAL TOXICITY/TERATOGENICITY (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	EPA Guidelines
GLP:	Yes
Year:	1992
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Oral gavage
Doses/concentration levels:	20, 100, 200 mg/kg/day (in corn oil)
Sex:	Female
Exposure period:	Day 6 through 15 of gestation
Frequency of treatment:	7 days/week
Control group and treatment:	Concurrent, received 5 ml/kg corn oil
Duration of test:	Day 20 of gestation
Statistical methods:	Continuous maternal and fetal data, including body weights, body weight gain, food consumption, number of fetuses, implantation sites and corpora lutea, were analyzed using one-way analysis of variance (ANOVA) followed by Dunnett's test. The Mann-Whitney U test was used to compare post-implantation loss and resorptions. Fetal sex ratios were analysed using the Chi-Square test. Fisher's Exact test was used to analyze the incidence and number of fetal malformations and variations utilizing the dam (litter) as the experimental unit.
Remarks:	Twenty-five female rats were assigned to each group. The animals were observed daily for clinical signs of toxicity. Body weights and food consumption were measured on gestation day 0, 6, 9, 12, 16, and 20. Surviving females were euthanized on gestation day 20 and subjected to cesarean section. Fetuses were individually weighed, sexed and examined for external, visceral and skeletal abnormalities.

Results

Maternal toxicity NOAEL:	= 20 mg/kg/day
Developmental toxicity NOAEL:	= 100 mg/kg/day
Actual dose received:	0, 20, 100, or 200 mg/kg/day
Maternal data:	There were no treatment-related mortality or clinical signs of toxicity. Mean maternal body weight gain and food consumption statistically reduced at the 100 and 200 mg/kg/day groups throughout the study. Greenish-blue discoloration of the amniotic sac was observed in a dose-related manner at the 100 and 200 mg/kg/day levels.

Fetal data:	Mean fetal body weight was statistically reduced at the 200 mg/kg/day level when compared to the control group. All other cesarean parameters were comparable among groups. No treatment-related malformations or developmental variations were observed.
Statistical results:	
Remarks:	
Conclusions	Oral gavage dosing with up to 200 mg/kg/day of mixed diethylbenzene (25340-1 7-4) did not produce a teratogenic response in rats. Maternal toxicity occurred at dosages that were lower than that which produced developmental toxicity.
Data Quality	
Reliability (Klimisch):	1A
Remarks:	Reliability without restriction; EPA guideline study.
Reference	Mercieca, M. D. 1992 Teratology Study in Rats with MCS 23 13 [mixed diethylbenzene] . Springborn Laboratories, Inc. Report No. 30344.228. Conducted for Monsanto Company.
Other Available Reports	<p>Saillenfait, A. M., Payan, J. P., Langonné. I., Gallissot, F., Sabaté, J. P., Beydon, D., and Fabry, J. P. (1999) Assessment of the developmental toxicity and placental transfer of 1,2-diethylbenzene in rats. Food Chemical Toxicol. 37: 1089-1096.</p> <p>2B: Reliable with restrictions; basic data given, comparable to guidelines/standards.</p> <p>MHW, Japan. 1993. Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for the OECD-SIDS program.</p> <p>4A: Not assignable; only short abstract available.</p>
Other	
Last changed:	September 4,200 1
Remarks:	

DEVELOPMENTAL TOXICITY/TERATOGENICITY (B)

Test Substance

Identity: 1,2-Diethylbenzene
Purity: >99%
Remarks:

Method

Method/guideline followed: Not stated
GLP: Not stated
Year:
Species: Rat
Strain: Sprague-Dawley
Route of administration: Oral gavage
Doses/concentration levels: 5, 15, 25, or 35 mg/kg/day
Sex: Female
Exposure period: Day 6 through 20 of gestation
Frequency of treatment: 7 days/week
Control group and treatment: Concurrent, received 2 ml/kg corn oil
Duration of test: Day 2 1 of gestation
Statistical methods: Number of implantation sites and live fetuses, food consumption and various body weights were analyzed by one-way analysis of variance, followed by Dunnett's test if differences were found. The frequencies of non-surviving implants, resorptions, males, and anomalies among litters were evaluated by using Dixon-Massey test. Rates of pregnancy and incidence of litters with alterations were analyzed by using Fisher's test. Where applicable, least-squares analysis was carried out.
Remarks: There were 28-29 female rats assigned to each group. All females were observed daily for clinical signs of toxicity. Food consumption was measured at 3-day intervals starting at gestation day (GD) 6. Maternal body weights were recorded on GDO, 6, 9, 12, 15, 18, 21. On GD 2 1, the females were euthanized and the uteri were removed and weighed. Uterine contents were examined to determine the number of implantation sites, resorptions, and dead/live fetuses. Live fetuses were weighed, sexed, and examined for external anomalies. Half of the live fetuses for each litter were examined for internal soft tissue changes and the other half were processed for skeletal staining.

Results

Maternal toxicity NOAEL: = 5 mg/kg/day
Developmental toxicity NOAEL: = 5 mg/kg/day
Actual dose received: 5, 15, 25, and 35 mg/kg/day
Maternal data: No animals died during the study. Maternal weight gain was significantly reduced during GD 6-9 in the ≥ 15 mg/kg dose groups, and for GD 18-2 1 in the 35 mg/kg dose group. Females dose with ≥ 15 mg/kg had

<p>Fetal data:</p> <p>Statistical results:</p> <p>Remarks:</p>	<p>significant dose-related decreases in maternal weight gain for GD 6-21 and in corrected weight gain. Maternal food consumption was significantly depressed during the initial and final three days of treatment at ≥ 15 mg/kg. Depression in food consumption persisted during GD 9-12 in the 25 mg/kg dose group, and during GD 9-12 and GD 15-18 in the 35 mg/kg dose group. Overall, food consumption on GD 6-21 was significantly decreased in the 25 and 35 mg/kg dose groups. There were no significant effects on the average number of implantations and live fetuses, on the incidence of non-surviving implants per litter, or on the fetal sex ratio. Fetal body weights in the ≥ 15 mg/kg dose groups were significantly reduced, and were dose-related. There was no evidence of a treatment-related effect in any malformations or variations.</p>
<p>Conclusions</p>	<p>Oral gavage dosing with up to 35 mg/kg/day 1,2-diethylbenzene produced reduced fetal body weights, but no teratogenic effects. Developmental toxicity occurred only at dosages that produced maternal toxicity.</p>
<p>Data Quality</p> <p>Reliability (Klimisch):</p> <p>Remarks:</p>	<p>2B</p> <p>Reliable with restrictions; basic data given, comparable to guidelines/standards.</p>
<p>Reference</p>	<p>Saillenfait, A. M., Payan, J. P., Langonné, I., Gallissot, F., Sabaté, J. P., Beydon, D., and Fabry, J. P. (1999) Assessment of the developmental toxicity and placental transfer of 1,2-diethylbenzene in rats. Food Chemical Toxicol. 37: 1089-1096.</p>
<p>Other Available Reports</p>	<p>Mercieca, M. D. 1992 Teratology Study in Rats with MCS 23 13 [mixed diethylbenzene]. Springborn Laboratories, Inc. Report No. 30344.228. Conducted for Monsanto Company.</p> <p>MHW, Japan. 1993. Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for the OECD-SIDS program.</p> <p>4A: Not assignable; only short abstract available.</p>
<p>Other</p> <p>Last changed:</p> <p>Remarks:</p>	<p>September 4, 2001</p>

